AD-A084 775 PROFESSIONAL STAFF ASSOCIATION OF LAC/USC MEDICAL CEN--ETC F/G 6/15
STUDIES ON THE BIOLOGY, VENOM AND ULTRASTRUCTURE OF SELECTED VE--ETC(U)
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PROFESSIONAL STAFF ASSOCIATION Los Angeles County/ University of Southern California Medical Center

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Final Technical Report to

OCEANIC BIOLOGY PROGRAM

OFFICE OF NAVAL RESEARCH

Submitted by

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Director, Laboratory of Neurological Research
Los Angeles County/University of Southern California
Medical Center,

Through the

Professional Staff Association

STUDIES ON THE BIOLOGY, VENOM AND ULTRASTRUCTURE OF SELECTED VENOMOUS FISHES, INCLUDING THE SCORPIONFISHES AND STINGRAYS.

OFFICE OF NAVAL RESEARCH
CONTRACT N00014-78-C-0206
(15)

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STUDIES ON THE BIOLOGY, VENOM AND ULTRASTRUCTURE OF SELECTED VENOMOUS FISHES, INCLUDING THE SCORPIONFISHES AND STINGRAYS

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Work Unit No. NR 104-793 Contract N00014-78-C-0206

During the past two years the principal research under the contract has been directed toward several problems:

1) A continued study of the ultrastructure of the venom apparatus of the stingrays Urobatis halleri and Dasytis sabina, and the scorpionfish Scorpaena guttata; 2) determination of certain physiopharmacologic changes provoked by the venom of the scorpionfishes; and 3) the histology and ultrastructure of skin from the soapfishes, Grammistidae.

With respect to current studies on the ultrastructure of the stingray venom apparatus, these have confirmed our earlier observations that the subunit distribution in stingray venom cell "microtubules" varies considerably within a single vacuole, in marked contrast to the tubulin polymers described as "convential cytoplasmic microtubules."

The improvement in the methods we have developed aided in the definition of these structures in thin sections and permits a more precise estimate of their diameter. While diameters are variable, they are substantially less than estimates for other intracellular microtubules. The chemistry of these microtubules has yet to be determined but by their anomalous location and fine structure it is suggested that they are polymers of non-tubulin protein(s). One protein component (150,000 daltons) was identified in Urobatis halleri venom. The variability in subunit

distribution in venom cell microtubules may indicate that a number of proteins are sequestered and polymerized within the vacuoles.

The improvements in the techniques we have developed for stabilizing the venoms of the scorpionfishes has permitted us to do a number of physiopharmacologic studies that heretofore have not been possible. Essentially, the procedure is as follows: Using the separation method previously developed in our laboratory, venom was extracted in 0.05 M sodium phosphate buffer, pH 7.4, and 10^{-3} M Cleland's reagent concentrated two-fold by ultrafiltration, using a UM-2 (Amicon) membrane under 75 psi N_2 pressure.

A cardiovascular survey model designed to study hypotension was employed to measure arterial and venous pressures; respirations; and blood pH, PO_2, PCO_2 and hematocrit; and total serum protein. The results indicated a fairly consistent pattern and has led to the employ of more definitive isolated-tissue segment preparations. This work is currently being completed. There is a close relationship between our findings and those we have observed in patients stung by the scorpionfishes.

Studies on several species of soapfishes (Grammistidae) indicated that there is a general pattern of three secretory cells in the epidermis of these fishes, as distinguished by histochemical staining and ultrastructural appearance. One secretory cell is a large, oval, PAS negative, Sudan black (SB) negative, homogenous, glassy appearing cell extending from the deep epithelial layers to the skin surface. Viewed with the electron microscope its contents appear as highly packed tiny granules. The second secretory cell is round and contains tightly packed large, PAS positive, SB negative granules, which empty through narrow openings. This cell is in the surface epithelium and is thought to be the mucus secreting cells found in all teleost skin. The third type

of secreting cell is the elongated cell extending from the deep epithelium to the surface, where it empties its irregular granules which are PAS negative and SB positive. It appears that the fish's toxin is probably a product of this third cell type with synergism with the second type.

The following papers, supported by the contract were published or are in press:

Chao, R.L.C., Parker, J.W., Russell, F.E. and Hashimota, Y. (1978) "Ultrastructure of the skin of the soapfish Grammistes sexlineatus." In, Toxins: Animal, Plant and Microbial. Rosenberg, P. (Ed.) p. 449-508, Pergamon Press, Oxford.

Smith, D.S., Cayer, M. and Russell, F.E. (1978) "Fine structure of stingray epidermis with special reference to a unique microtubular component of the venom secreting cells." In, Toxins: Animal, Plant and Microbial. Rosenberg, P. (Ed.) p. 565-582, Pergamon Press: Oxford.

Russell, F.E. (1978) Hazardous marine life. Part I. Venomous maring animals. Hyperbaric & Undersea Medicine 1: 1-8.

Russell, F.E., Smith, D.S., Cayer, M. and Gonzalez, H.C. (1978) Behavior, ecology and toxicity of venomous marine fishes. ONR Prog. Rept. ACR-228, p. 91 December (Abst.).

Maretic, Z., Russell, F.E. and Ladavac, J. (1979) Epidemic of stings by the jellyfish Pelagia noctiluca in the Adriatic.

Abstract of the 6th International Symposium on Animal, Plant and Microbial Toxins, Uppsala, August. Toxicon 17, 115.

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Epidemiologija I Terapije Uboda I Ujeda Otrovnih Zivotinja U. Sad. II Kongres Udruzenja Toksikologa Jugoslavije, Portoroz, Jugoslavije, p. 27.

Russell, F.E., Smith, D.S., Cayer, M. and Gonzalez, H.C. (1979)
Behavior, Ecology and Toxicity of Venomous Marine Fishes. ONR Prog. Rept. ACR-230, p. 99 December. (Abst.)

Russell, F.E. (1980)
The marine organism sting mystery. (Questions and Answers) J.A.M.A. 243: 1573.

Coats, J.A., Pattabhiraman, T.R., Russell, F.E. and Gonzalez, H.C. (1980)
Some physiopharmacologic properties of scorpionfish venom. Proc. west. Pharmacol. Soc. (In Press)

Sloan, C. and Russell, F.E. (1980)
Ultrastructure of the venom apparatus of the scorpionfish Scorpaena guttata. Toxicon. (In Press)

Smith, D.S., Cayer, M. and Russell, F.E. (1980)
Tannic acid staining of "microtubules" in venom-secreting cells of the stingray. Toxicon. (In Press)

Dymsza, H., Shimizu, Y., Russell, F.E. and Graham, H.D. (1980)
"Poisonous Marine Animals." In, The Safety of Foods. Graham, H.D., (Ed.) p. 625-651, AVI: Westport, Connecticut.

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: 1 - Final
2. GOVT ACCESSION NO.: AD-A084 775
3. RECIPIENT'S CATALOG NUMBER:

4. TITLE (and Subtitle): Studies on the biology, venom and ultrastructure of selected venomous fishes including the scropionfishes and stingrays

5. TYPE OF REPORT & PERIOD COVERED: Final - Technical

6. PERFORMING ORG. REPORT NUMBER: 1

7. AUTHOR(s): Findlay E. Russell, M.S., Ph.D.

8. CONTRACT OR GRANT NUMBER(s): N00014-78-C-0206

9. PERFORMING ORGANIZATION NAME AND ADDRESS: Professional Staff Association of the LAC/USC Medical Center, 1739 Griffin Ave., Los Angeles, CA. 90031

10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS:

11. CONTROLLING OFFICE NAME AND ADDRESS:

12. REPORT DATE: April 25, 1980

13. NUMBER OF PAGES: 2

14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): Commanding Officer, Office of Naval Research Branch Office, 1030 East Green Street, Pasadena, CA. 91101

15. SECURITY CLASS. (of this report): Unclassified

15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT (of this Report): Unlimited

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report):

18. SUPPLEMENTARY NOTES:

19. KEY WORDS (Continue on reverse side if necessary and identify by block number):

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

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DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE S/N 0102-014-6601

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

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